IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Vega *et al.*	Art Unit	: 1631
Patent No.	: 7,647,184	Examiner	: Lin, Jerry
Issue Date	: January 12, 2010	Conf. No.	: 7196
Serial No.	: 10/022,249	Cust. No.	: 77202
Filed	: December 17, 2001		
Title	: HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS		

Attn.: Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION

Dear Sir:

Pursuant to C.F.R. § 1.322 & 1.323, the patentee respectfully requests that a Certificate of Correction be issued for the above referenced patent to correct the following errors:

IN THE CLAIMS

Please replace claims 9, 15, 19 and 26 with the following amended claims:

9. The method of claim 1, wherein the pre-selected amino acid is selected from among Arg (R), Asn (N), Asp (D), Cys (C), Gln [(O)] (Q), Glu (E), His (H), Ile (I), Leu (L), Lys (K), Met (M), Phe (F), Thr (T), Trp (W), Tyr (Y) and Val (V).

15. The process of claim 1, wherein:

in step (b) the nucleic acid molecules comprise viral vectors, and the ~~methods~~ method further comprises assessing the titer of the viral vectors in each set of cells; and

the predetermined property or an activity is selected from among a chemical, a physical and a biological property of the target protein.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
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Date of Deposit: February 2, 2010
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Certificate of Correction Branch, Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

Christopher M. Ochs

19. The process of claim 18, wherein the Hill analysis, comprises:

(a) preparing a sample of each nucleic acid molecule or a plasmid or vector that comprises each nucleic acid molecule (biological agent), wherein each sample is obtained by a serial dilution of the molecules or vector or plasmid at a concentration R1;

(b) incubating each sample of the dilution obtained in (a) with the host cells (target cells) at a constant concentration R2;

(c) determining a P product from the reaction R1 + R2, at a t moment, in each ~~the~~ sample; and

(d) preparing a theoretical curve H from the experimental points R1 and P, for each biological agent by iterative approximation of parameters of the reaction R1 + R2 → P, at the t moment, in accordance with the equation:

$$P = P_{max} (\pi R1)^r / (\kappa + (\pi R1)^r) \qquad r=1,\ldots,n \qquad (2)$$

in which:

R1 represents the biological agent concentration in a sample from the scale;

R2 is concentration of target cells (in vitro or in vivo)

P (output) represents the product from the reaction R1 + R2 at a t moment;

P_{max} represents the reaction maximal capacity;

κ represents, at a constant R2 concentration, the biological system for responding to the biological agent (resistance constant R2);

r represents a dependent coefficient of R1 and corresponds to the Hill coefficient; and

π represents the intrinsic power of the R1 biological agent to induce a response in the biological system (P production at the t moment); and

(e) sorting the κ and π values obtained in (d) for each protein encoded by the nucleic acid molecules or plasmids or vectors and the cells, and then ranking according to the values thereof.

26. The method of claim 22, wherein the pre-selected amino acid is selected from among ~~encoding~~ Arg (R), Asn (N), Asp (D), Cys (C), Gln [(O)] (Q), Glu (E), His (H), Ile (I), Leu (L), Lys (K), Met (M), Phe (F), Thr (T), Trp (W), Tyr (Y) and Val (V).

REMARKS

A Certificate of Correction (Form PTO-1050) incorporating the above changes is included with this Request. Since not all the errors are those of the Patent Office, the Office is hereby authorized to charge any fees due herein to Deposit Account No. 02-1818.

IN THE CLAIMS:

This Certificate of Correction also seeks to correct obvious typographical errors in the Claims introduced by the PTO. Claims 9 and 26 are amended to correct the same typographical error in which "O" was recited instead of "Q" as the one letter amino acid code for glutamine (Gln), such that the phrase now reads as —Gln (Q),—.

Additionally, this Certificate of Correction seeks to correct obvious typographical and grammatical errors in Claims 15, 19 and 26.

Accordingly, none of the requested changes constitute new matter. Patentee respectfully requests correction of errors by issuance of a Certificate of Correction.

Respectfully submitted,

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SUBSTITUTE FORM PTO/SB/44 (5-03)

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. .: 7,647,184

APPLICATION NO .: 10/022,249

DATED .: JANUARY 28, 2010

INVENTOR(S) .: VEGA ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE CLAIMS:

Please replace Claim 9 with the following amended Claim:

Column 78, lines 23-26

9. The method of claim 1, wherein the pre-selected amino acid is selected from among Arg (R), Asn (N), Asp (D), Cys (C), Gln (Q), Glu (E), His (H), Ile (I), Leu (L), Lys (K), Met (M), Phe (F), Thr (T), Trp (W), Tyr (Y) and Val (V).

Please replace Claim 15 with the following amended Claim:

Column 78, lines 59-65

15. The process of claim 1, wherein:
in step (b) the nucleic acid molecules comprise viral vectors, and the method further comprises assessing the titer of the viral vectors in each set of cells; and
the predetermined property or an activity is selected from among a chemical, a physical and a biological property of the target protein.

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It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Please replace Claim 19 with the following amended Claim:

Column 79, line 33 to Column 80, line 4

19. The process of claim 18, wherein the Hill analysis, comprises:

(a) preparing a sample of each nucleic acid molecule or a plasmid or vector that comprises each nucleic acid molecule (biological agent), wherein each sample is obtained by a serial dilution of the molecules or vector or plasmid at a concentration R1;

(b) incubating each sample of the dilution obtained in (a) with the host cells (target cells) at a constant concentration R2;

(c) determining a P product from the reaction R1 + R2, at a t moment, in each sample; and

(d) preparing a theoretical curve H from the experimental points R1 and P, for each biological agent by iterative approximation of parameters of the reaction R1 + R2 → P, at the t moment, in accordance with the equation:

$$P = Pmax\ (\pi R1)r / (\kappa + (\pi R1)r) \qquad r=1,\ldots,n \qquad (2)$$

in which:

R1 represents the biological agent concentration in a sample from the scale;
R2 is concentration of target cells (in vitro or in vivo)
P (output) represents the product from the reaction R1 + R2 at a t moment;
Pmax represents the reaction maximal capacity;
κ represents, at a constant R2 concentration, the biological system for responding to the biological agent (resistance constant R2);

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r represents a dependent coefficient of R1 and corresponds to the Hill coefficient; and

π represents the intrinsic power of the R1 biological agent to induce a response in the biological system (P production at the t moment); and

(e) sorting the κ and π values obtained in (d) for each protein encoded by the nucleic acid molecules or plasmids or vectors and the cells, and then ranking according to the values thereof.

Please replace Claim 26 with the following amended Claim:

Column 82, lines 4-8

26. The method of claim 22, wherein the pre-selected amino acid is selected from among Arg (R), Asn (N), Asp (D), Cys (C), Gln (Q), Glu (E), His (H), Ile (I), Leu (L), Lys (K), Met (M), Phe (F), Thr (T), Trp (W), Tyr (Y) and Val (V).

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